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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/405,454	03/15/1995	JOHN B. SULLIVAN	4249.0002-05	6004

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EXAMINER
SCHWADRON, RONALD B

ART UNIT	PAPER NUMBER
1644	48

DATE MAILED: 06/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	08/405,454	SULLIVAN ET AL.	
	Examin r	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the c ver sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-42 and 50-55* is/are pending in the application.

4a) Of the above claim(s) *53-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-42 and 50-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. It is noted that claims 48 and 49 were already previously pending and have been cancelled. Therefore, claims 48-53 in the amendment filed 3/31/2003 have been renumbered as 50-55.

2. It is noted that claims drawn to methods of treatment or Fab2 antivenom compositions **were not present in the Appeal Brief filed by applicant and were not addressed by the BPAI decision mailed 1/29/2003**.

Newly submitted claims 53-55 are directed to inventions that are independent or distinct from the invention originally claimed for the following reasons.

The invention under consideration (antivenom comprising Fab antisera) is classified in Class 424, subclass 177. Group II is drawn to a method of treatment, classified in Class 424, subclass 158.1. Group III is drawn to an antivenom comprising Fab2 classified in Class 424, subclass 133. The invention currently under consideration and Group II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case, the product as claimed can be used in a materially different process such as immunoassay or immunopurification procedures.

The invention currently under consideration and Group III are different products. There are structurally and functionally distinct, have different uses and different pharmacological activities. Therefore they are novel and unobvious in view of each other and are patentably distinct. Because these inventions are distinct for the reasons given above and the search required for any group from Groups I-III is not required for any other group from Groups I-III and Groups I-III have acquired a separate status in the art as shown by their different classification and divergent subject matter, restriction for examination purposes as indicated is proper.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 53-55 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

In addition the MPEP section 1214.06 states:

III. CLAIMS REQUIRE ACTION

If the decision of the Board is an affirmance in part and includes a reversal of a rejection that brings certain claims up for action on the merits, such as a decision reversing the rejection of generic claims in an application or ex parte reexamination proceeding containing claims to nonelected species not previously acted upon, the examiner will take up the application or reexamination proceeding for appropriate action on the matters thus brought up. ***However, the application or reexamination proceeding is not considered open to further prosecution except as to such matters.***

3. Claims 40-42,50-52 are under consideration. Claims 40-42 were amended. Claims 50-52 are newly added. Claims 45-47 have been cancelled. The rejection of claims 45-47 for the reasons elaborated in the previous Office Actions was affirmed in the decision of the BPAI mailed 1/29/2003.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 40-42,50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sullivan in view of Coulter as per the rejection enunciated by the BPAI in the decision mailed 1/29/2003. Applicants arguments have been considered and deemed not persuasive.

Regarding applicants comments, the composition rendered obvious by the instant rejection would neutralize the lethality of the venom of a snake of the Crotalus genus because it contains the same ingredient as that recited in the claims (eg. Fab which binds Crotalus venom). Regarding the new preamble of claim 40, it is unclear as why said preamble should be given any more weight than the old preamble, because both preambles merely refer to an intended use for the claimed invention. IgG(T) is horse derived immunoglobulin (see page 6 of the BPAI decision mailed 1/29/2003, page 6, footnote).

6. Claim 51 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sullivan in view of Coulter as applied to claims 40-42,48 above, and further in view of Gratzner et al. (US Patent 4,529,700).

The previous rejection renders obvious the claimed invention except for use of lyophilized antibody. Gratzner et al. disclose use of lyophilized antibody (see column 5, penultimate paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection renders obvious the claimed invention except for use of lyophilized antibody whilst Gratzner et al. disclose use of lyophilized antibody. Lyophilization was used as a means to store the antibody (eg. the antibody could be frozen or lyophilized, see column 5, penultimate paragraph).

Regarding applicants comments, lyophilized antibodies were well known in the prior art.

7. Claim 52 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sullivan in view of Coulter as applied to claims 40-42,48 above, and further in view of Reckel et al. (US Patent 4,595,654).

The previous rejection renders obvious the claimed invention except for use of thimerosal. Reckel et al. disclose an antibody preparation containing thimerosal (see

column 13 lines 64-66). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection renders obvious the claimed invention except for use of thimerosal whilst Reckel et al. disclose use of thimerosal in an antibody preparation. Thimersol is an art known preservative.

Regarding applicants comments, antibody preparations containing thimersol were known in the art.

8. The following rejections respond to the newly amended claims as actually encompassing an antivenom which is actually used to treat snakebite.

9. Claims 40-42,50 are rejected under 35 U.S.C. § 103 as being unpatentable over Sullivan et al. in view of Coulter et al. and Smith et al. as evidenced by Stedman's Medical Dictionary (1977).

Sullivan et al. teach purified antivenin polyvalent antibodies derived from horse hyperimmune antisera against venom of the Crotalus genus (see *Methods* section, pages 185-187). These antibodies are predominantly IgG(T), because that is the predominant isotype found in hyperimmune horse antisera. A routineer would have immunized horses to produce said hyperimmune antisera because this is the art recognized procedure for producing antivenin. Sullivan et al. do not teach a F(ab) containing antivenin. The amendment filed 5/4/98, pages 3 and 4 establishes that the art recognized that the terms "antivenin" and "antivenom" refer to the same product.

Coulter et al. teaches a method for producing F(ab) fragments that are free of Fc (see abstract). Coulter et al. teaches a composition of F(ab) fragments of antibody against textilotoxin (a snake toxin) (see pages 201-203). Stedman's Medical Dictionary defines antivenin as "an antitoxin specific for an animal or insect toxin"(page 94). Therefore the composition taught by Coulter et al. is an antivenin. The F(ab) composition (page 201, third paragraph) was derived from polyclonal antisera against textilotoxin (page 199, second paragraph). The F(ab) produced by said method were free of Fc and extraneous protein (see Abstract). A routineer would have assayed for Fc by immunoelectrophoresis using anti-Fc antibodies or any other art recognized procedure.

Smith et al. teaches the advantages of F(ab) fragments for the neutralization and clearance of toxic substances in therapeutic applications (see page 393, first paragraph, *Discussion* section). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have produced antivenom compositions consisting of F(ab) fragments because Sullivan et al. teach purified antivenin polyvalent antibodies derived from horse hyperimmune antisera against venom of the Crotalus genus, Coulter et al. teaches a method for producing antivenin F(ab) fragments that are free of Fc, and Smith et al. teaches the advantages of F(ab) fragments for the neutralization and clearance of toxic substances in therapeutic applications. One of ordinary skill in the art would have been motivated to do the aforementioned because Smith et al. teaches that,

"Relatively rapid clearance of Fab fragments can be used to advantage when the objective is rapid neutralization and clearance of a toxic substance, and purified sheep digoxin specific Fab fragments have been utilized clinically for the reversal of advanced digoxin intoxication. This therapeutic approach is based on similar binding properties and the postulated lesser immunogenicity of Fab compared with IgG. For urgent clinical situations such as life threatening digitalis-toxic cardiac arrhythmias, the present study indicates that Fab has another important advantage-more rapid and extensive distribution to its presumed site of action in the interstitial space." (page 393). Further motivation is provided by the teaching of Coulter et al. that F(ab) antivenin can be made and that said antivenin work in vivo to neutralize snake toxins (see page 202, third paragraph). In addition, Sullivan et al. teach that reducing the immunogenicity of polyvalent horse antivenin is an important goal, due to immune reactions that limit the clinical efficacy of antivenin preparations which contain only partially purified hyperimmune horse antisera (see page 185, first paragraph).

Applicants arguments are addressed in the Examiners Answer filed 5/8/2000.

10. Claim 51 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sullivan et al. in view of Coulter et al. and Smith et al. as evidenced by Stedman's Medical Dictionary (1977) as applied to claims 40-42,48 above, and further in view of Gratzner et al. (US Patent 4,529,700).

The previous rejection renders obvious the claimed invention except for use of lyophilized antibody. Gratzner et al. disclose use of lyophilized antibody (see column 5,

penultimate paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection renders obvious the claimed invention except for use of lyophilized antibody whilst Gratzner et al. disclose use of lyophilized antibody. Lyophilization was used as a means to store the antibody (eg. the antibody could be frozen or lyophilized, see column 5, penultimate paragraph).

Regarding applicants comments, lyophilized antibodies were well known in the prior art.

11. Claim 52 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sullivan et al. in view of Coulter et al. and Smith et al. as evidenced by Stedman's Medical Dictionary (1977) as applied to claims 40-42,48 above, and further in view of Reckel et al. (US Patent 4,595,654).

The previous rejection renders obvious the claimed invention except for use of thimerosal. Reckel et al. disclose an antibody preparation containing thimerosal (see column 13 lines 64-66). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection renders obvious the claimed invention except for use of thimersol whilst Reckel et al. disclose use of thimerosal in an antibody preparation. Thimersol is an art known preservative.

Regarding applicants comments, antibody preparations containing thimersol were known in the art.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 51 and 52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the inventions of claim 51 or 52. Applicant has indicated that said limitations find support in the recitation of ACP on page 15, line 28 of the specification. However, said line of the specification and the passages following it disclose use of ACP (a commercial antivenom preparation containing intact antibody) to prepare F(ab) fragments. The preparation was reconstituted with fluid prior to use. The F(ab) fragments that are derived were in the liquid phase. Furthermore, any thimerosal would be removed in the affinity purification procedure. Thus, the prepared F(ab) are not lyophilized or found in thimerosal. There is no disclosure in the specification of the claimed Fab antivenom containing thimerosal or in a lyophilized form. There is no support in the specification as originally filed for the claimed invention (eg. the claimed invention constitutes new matter).

14. No claim is allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. No claim is allowed.

17. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the

Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 308-4242.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644